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From: Lawton, Alison [Alison.Lawton@genzyme.com]  
Sent: Thursday, June 13, 2002 9:27 AM  
To: 'FDADocket'  
Subject: Docket No. 02N-0169 - Request to make presentation at public hearing

(Docket Number 02N-0169)  
Federal Register Notice- Combination Products Containing Live Cellular Components; Public Hearing

Re: Request for Public Presentation by Genzyme Corporation

Genzyme Corporation is requesting an opportunity to participate in the above mentioned Part 15 hearing and would like to make a public comment relating to the specific products under discussion. Genzyme Corporation currently has a commercial product, Epicel, which fits the description of a wound healing combination product containing live cellular components. Epicel is indicated for use in patients with deep dermal or full thickness burns comprising total body surface area of >30% and in patients with congenital pigmented nevus. Epicel is a commercial product, currently under review by CDRH as a Humanitarian Use Device but is also designated as a xenotransplantation product because the processing uses a murine 3T3 feeder cell line for growing the autologous human keratinocytes. Genzyme is also active in continuing to develop tissue and cell therapies and any decision made by the Agency regarding the future regulation of these products will have a direct implication for the organization and future potential products being developed.

The information requested in the notice for participation is provided below:

1. Contact Details:

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2. Brief Summary of Presentation

Overview of Epicel and it's regulatory history.  
Epicel was originally introduced to the market in 1987 as an unregulated device. It is a cultured epidermal autograft

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with proliferative cultured autologous keratinocytes attached to petrolatum gauze backing. In October 1997, it was designated as a wound-healing product and regulated as a device under CDRH jurisdiction. It is currently considered a combination product due to the presence of the murine feeder cell layer that is encompassed by CBER's definition of xenotransplant products.

Genzyme comment on each of the considerations listed in Section III, points 1-3.

#### Potential Public Health Concerns:

We agree that any potential for public health concern needs to be addressed in a consistent manner within the Agency. The primary concern is the potential transmission of infectious agents that could result from such issues as tissue sourcing and cross-contamination from improper or uncontrolled processing.

#### Manufacturing Controls:

Genzyme has significant experience with the manufacturing of cell products both through the manufacture of Epicel as well as Carticel, an autologous human chondrocyte product regulated by CBER. The manufacture of these cell therapy products needs to be in strict accordance with Good Manufacturing Practices with an emphasis on issues pertaining to cell products such as control over sourcing of materials, process validation, environmental control, containment during processing, patient identification and tracking by lot and product release testing.

#### Assessment of Safety and Efficacy:

Safety and efficacy of these products should be demonstrated in controlled clinical trials. However, the Agency needs to develop a flexible approach to trial design given that placebo controlled clinical trials may not always be feasible or ethical.

#### Mode of Action, Designation and Regulatory

Process:

Currently approved commercial products consisting of living human cells in combination with a device matrix and intended for wound healing should remain within CDRH. However any new products or new indications for currently approved products should be regulated as outlined below.

Genzyme believes that the Agency should have a consistent approach to the regulation of all products containing human living cells. Decisions about regulation of such products should be based primarily

on whether a product contains living cells. In most cases of products containing living cells, the product should be regulated by CBER in the new Office of Cell, Tissue and Gene Therapy. Any scaffold, matrix or biomaterial supporting the cells would in most cases be considered as a delivery system for optimizing or facilitating the effect of the cell being delivered. Such delivery systems should be reviewed by CDRH as a consult to CBER for that component of the final product. This would ensure that the appropriate expertise is applied within the context of a single biologics approval for the final product.

The processes for review of combination products containing both living cells and a device component, where CBER would be the lead review and CDRH provide consult review, should be clearly defined with performance targets and these should be made transparent to all stakeholders in the form of guidances.

Genzyme also encourages continued communication between FDA and the European Authorities with an aim of developing a harmonized approach to the regulation of these types of products.

3. Time Requested for Presentation

15-20 minutes

Genzyme Corporation has significant expertise and experience with products consisting of living cells and looks forward to being able to actively participate by providing public comment during the meeting.